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ARIAD PHARMACEUTICALS, INC.
ARIAD GENE THERPEUTICS, INC.
26 LANDSDOWNE ST.
CAMBRIDGE, MA 02139

EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,062	CLACKSON ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	MAIL

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/9/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 11/18/2003. Claim 1 is pending and under examination in the instant application.

Specification

The disclosure is objected to because of the following informalities: the first paragraph of the specification should be updated to acknowledge the issued patent to US Patent Application No. 09/781,804.

Appropriate correction is required.

Priority

This application claims priority to USSN 09/781,804, filed 2/12/01 (now US Patent 6,649,595), which is a divisional application of USSN 09/012,097, filed 1/22/1998 (now US Patent 6,187,757) as a continuation in part of USSN 08/791,044 filed 1/28/1997 (now abandoned), which itself is a continuation-in-part of USSN 09/481,941, filed 6/7/1995 (now abandoned), and of USSN 60/015,502, filed 2/9/1996 and claims the priority benefit of International Application No. PCT/US/09948, filed internationally 6/7/1996. However, Examiner has found no

support for the structure of formula 1 in claim 1 of the instant application in USSN 08/481,941. Therefore, the benefit of priority is only extended as far back as USSN 09/012,097, filed 1/22/1998.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 recites a "method for multimerizing chimeric proteins in cells which comprises:

(a) providing cells which contain:

(i) a first recombinant nucleic acid encoding a first chimeric protein which binds to rapamycin or an analog thereof and which comprises at least one FKBP domain and at least one protein domain heterologous thereto, wherein the FKBP domain comprises a peptide sequence selected from:

(1) a naturally occuring FKBP

(2) a variant of naturally occuring FKBP in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids,

(3) an FKBP encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FKBP of (i) or (ii);

(ii) a second recombinant nucleic acid encoding a second chimeric protein which forms a complex with both (a) rapamycin or a rapamycin analog and (b) the first chimeric protein, and which comprises at least one FRB domain and at least one domain heterologous thereto, wherein the FRB domain comprises a peptide sequence selected from:

(1) a naturally occuring FRB domain,

(2) a variant of a naturally FRB domain in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids,

(3) an FRB domain encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FRB of (iv) or (v)" in lines 1-28.

Claim 1 is objected to because the acronyms FKBP and FRB are not spelled out upon their first occurrence within the claim in lines 9 and 21, respectively. Claim 1 is also objected to because "occurring" is misspelled once in line 13, once in line 14 and once in line 24, and it appears to be altogether missing in line 25. Claim 1 is also objected to because the designated subsections in lines 17, 24-25 and 27-28 are improperly labeled. Claim 1 should instead recite a "method for multimerizing chimeric proteins in cells which comprises:
(a) providing cells which contain:

(i) a first recombinant nucleic acid encoding a first chimeric protein which binds to rapamycin or an analog thereof and which comprises at least one ~~FKBP~~ FK506-binding protein (FKBP) domain and at least one protein domain heterologous thereto, wherein the FKBP domain comprises a peptide sequence selected from:

(1) a naturally ~~occuring~~ occurring FKBP

(2) a variant of naturally ~~occuring~~ occurring FKBP in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids,

(3) an FKBP encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FKBP of [[(i)]] (1) or [[(ii)]] (2);

(ii) a second recombinant nucleic acid encoding a second chimeric protein which forms a complex with both (a) rapamycin or a rapamycin analog and (b) the first chimeric protein, and which comprises at least one [[FRB]] FKBP:rapamycin binding (FRB) domain and at least one domain heterologous thereto, wherein the FRB domain comprises a peptide sequence selected from:

[[(1)]] (4) a naturally ~~occuring~~ occurring FRB domain,

[[(2)]] (5) a variant of a naturally occurring FRB domain in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids,

[[(3)]] (6) an FRB domain encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FRB of [[(iv)]] (4) or [[(v)]] (5)" in lines 1-28.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FKBP of (i) or (ii)" in lines 16-17 and "a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FRB of (iv) or (v)" in lines 27-28. Claim 1 is vague and indefinite in that it is not clear what requirements are necessary for a sequence to be "capable" of selectively hybridizing to a DNA sequence. Claim 1 should instead recite "…a DNA sequence which selectively hybridizes…" in both instances.

Claim 1 futher recites "…(b) contacting the cells with an improved rapalog which forms a complex containing itself and at least one molecule of each of the first and second chimeric proteins, where the improved rapalog has an immunosuppressive effect less than 0.01 times that of rapamycin and comprises the substructure of formula 1…" in lines 32-35. Claim 1 is vague and indefinite in that it is unclear what the improvement to the rapalog is. Is the rapalog improved in that it has a lower immunosuppressive effect or is there some other measure being used as a basis for the improvement?

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an

invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,187,757 (henceforth the '757 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim of the instant application is a genus claim that is anticipated by the species claim of the '757 patent.

Specifically, claim 1 of the instant application and claim 1 of the '757 patent are both drawn to a method for multimerizing chimeric proteins in cells which comprises:

(a) providing cells which contain:

(i) a first recombinant nucleic acid encoding a first chimeric protein which binds to rapamycin or an analog thereof and which comprises at least on FK506-binding protein (FKBP) domain and at least one protein domain heterologous thereto, wherein the FKBP domain comprises a peptide sequence selected from: (1) a naturally occurring FKBP; (2) a variant or a naturally occurring FKBP in which up to 10 amino acid residues have been deleted, inserted or replaced with substitute amino

acids; (3) an FKBP encoded by a DNA sequence capable of hybridizing to a DNA sequence encoding an FKBP of (1) or (2);

(ii) a second recombinant nucleic acid encoding a second chimeric protein which forms a complex with both (a) rapamycin or a rapamycin analog and (b) the first chimeric protein, and which comprises at least one domain heterologous thereto, wherein the FRB domain comprises a peptide sequence selected from: (4) a naturally occurring FRB domain, (5) a variant of a naturally occurring FRB domain in which up to 10 amino acid residues habe been deleted inserted or replace with substitute amino acids (6) an FRB domain encoded by a DNA sequence which selectively hybridizes to a DNA sequence encoding an FRB of (4) or (5); and

(b) contacting the cells with a rapalog which forms a complex containing itself and at least one molecule of each of the first and second chimeric proteins, where the rapalog has an immunosuppressive effect less than 0.01 times that of rapamycin and comprises the substructure of formula 1. However, claim 1 of the instant application is broader in scope that claim 1 of the '757 patent in that it encompasses in (a)(i)(3) any FKBP encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FKBP of (1) or (2), whereas patent '757 is limited to any FKBP encoded by a DNA sequence which

selectively hybridizes to a DNA sequence encoding an FKBP of (1) or (2). Similarly, claim 1 of the instant application is broader in scope than claim 1 of the '757 patent because it encompasses in (a)(ii)(6) an FRB domain encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FRB of (4) or (5), whereas patent '757 is limited to an FRB domain encoded by a DNA sequence which selectively hybridizes to a DNA sequence encoding an FRB of (4) or (5).

Claim 1 of the instant application also differs from claim 1 of the '757 patent in that claim 1 of the instant application recites an "improved rapalog" in line 32 and in line 34 whereas the rapalog of claim 1 of the '757 patent simply recites "rapalog" in the same instances; both the improved rapalog of the instant application and the "rapalog" of the '757 patent appear, however, to be identical in that both comprise the same claimed substructure of formula 1 and both have an immunosuppressive effect less than 0.01 times that of rapamycin. For purposes of this rejection only, Examiner has interpreted there to be no difference between the "improved rapalog" of the instant application and the "rapalog" of the '757 patent.

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

claim 1 of U.S. Patent No. 6,649,595 (henceforth the '595 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim of the instant application is a genus claim that is anticipated by the species claim of the '595 patent.

Specifically, claim 1 of the instant application and claim 1 of the '595 patent are both drawn to a method for multimerizing chimeric proteins in cells which comprises: (a) providing cells which contain: (i) a first recombinant nucleic acid encoding a first chimeric protein which comprises at least on FKBP domain wherein the FKBP domain comprises a peptide sequence selected from : (1) a naturally occurring FKBP or (2) a variant thereof in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids. However, claim 1 of the instant application encompasses a third and broader category of FKBP domains comprising a peptide sequence from "(3) an FKBP encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FKBP" of (1) or (2).

Similarly, claim 1 of the instant application and claim 1 of the '595 patent are both drawn to a method for multimerizing chimeric proteins in cells which comprises: (a) providing cells which contain: (ii) a second recombinant nucleic acid encoding a

second chimeric protein which comprises at least one FRB domain wherein the FRB domain comprises a peptide sequence selected from : (4) a naturally occurring FRB or (5) a variant thereof in which up to 10 amino acid residues have been deleted, inserted, or replaced with substitute amino acids. However, claim 1 of the instant application encompasses a third and broader category of FRB domains comprising a peptide sequence from "(3) an FRB domain encoded by a DNA sequence capable of selectively hybridizing to a DNA sequence encoding an FRB" of (4) or (5).

Claim 1 of the instant application also differs from claim 1 of the '595 patent in that claim 1 of the instant application recites and "improved rapalog" in line 32 and in line 34 whereas the rapalog of claim 1 of the '595 patent simply recites "rapalog" in the same instances; both the improved rapalog of the instant application and the "rapalog" of the '595 patent appear, however, to be identical in that both comprise the same claimed substructure of formula 1 and both have an immunosuppressive effect less than 0.01 times that of rapamycin. For purposes of this rejection only, Examiner has interpreted there to be no difference between the "improved rapalog" of the instant application and the "rapalog" of the '595 patent.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter A. Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office.)

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

March 3, 2006

NANCY VOGEL
PRIMARY EXAMINER